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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,556	01/05/2000	Yuman Fong	MSKP031USNP	4110

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,556	FONG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5/23/05.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-37 and 41-56 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-37 and 41-56 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/23/05 has been entered. Applicant's amendment and response also received on 5/23/05 has been entered. Claims 38-40 have been canceled. Claims 1-37, and 41-56 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Double Patenting

Claims 1-22 and 41-56 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,051,428 (4/18/00), hereafter referred to as the '428 patent. Since the applicants have not traversed the grounds of rejection, the rejection of record **stands**. However, it is noted that applicants have again indicated their willingness to file a terminal disclaimer over US Patent 6,051,428 upon indication that the claims are allowable over the prior art of record.

Claim rejections - 35 U.S.C. 112

The rejection of record of claims 4-6, and 41-53 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of applicant's amendments to claims 4 and 5. However, please note that these amendments have resulted in a new objection to claim 4, and a new grounds of rejection of claim 5 under 35 U.S.C. 112, second paragraph.

Claim 5 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 as amended appears to missing a method step. The claim now recites, "comprising the step one or more species of herpes simplex virus .....". However, no actual method step is recited. Further, as amended, the claim lacks antecedent basis for "transduced tumor cells". From the context of the claim, it would appear that the claim should read, " comprising the step of transducing tumor cells with one or more species of herpes simplex virus". If this is indeed correct, it is suggested that the claim be amended to include this language.

Claim Objections

Claims 4, 6, and 41-53 are newly objected to because of the following informalities: claim 4, as amended is missing the word "of" between the words "step" and "administering" in line 2 of the claim. Appropriate correction is required.

Claims rejections - 35 U.S.C. 101

The previous office action withdrew the rejection of claims 36 and 37 under 35 U.S.C. 101 for non-statutory subject matter. However, in view of applicant's comments on page 7 of the response that the claims read on tumor cells "wherever they may exist, including in a host organism", the rejection of claims 36-37 has been reapplied below.

Claims 36-37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims recite tumor cells transduced according to the method of claim 1, or tumor cells transduced with a mixture according to claim 23. Claim 1 recites a method for producing transduced tumor cells which reads on both *in vivo* and *ex vivo* transduction, see claims 2 and 3. Thus, tumor cells made using this method could be *in vivo* or *ex vivo*. Claim 36, therefore, clearly reads on tumor cells present in any mammal, including a human. As such, the claim encompasses a human being, which is not statutory subject matter. Applicant's comments on page 7 of the response seem to agree with this interpretation of the claims, as they state that the claims read on tumor cells "wherever they may exist, including in a

host organism". It is suggested that the claims be amended to recite, "isolated tumor cells", or "tumor cells *ex vivo*" in order to overcome this rejection.

Claims rejections - 35 U.S.C. 102

The rejection of claims 1-3, and 7-40 under 35 U.S.C. 102(e) over U.S. Patent No. 6,344,445, 2/5/02, hereafter referred to as Boursnell et al, is maintained over pending claims 1-3 and 7-38 and withdrawn over canceled claims 38-40. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant reiterates their argument that Boursnell fails to demonstrate "possession" by failing to provide sufficient "written description" under 35 U.S.C. 112, first paragraph. The previous office action directed the applicants to the section of the MPEP which clearly sets forth the appropriate standard for determining whether the disclosure of a prior art reference meets the level of an anticipatory reference under 35 U.S.C. 102. MPEP 2121.01 states that "'In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... .'" *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d

531, 226 USPQ 619 (Fed. Cir. 1985). *In re Donohue* further states, " the fact that an author of a publication did not attempt to make the compound disclosed, without more, will not overcome a rejection based on that publication". Neither the MPEP nor *In re Donohue* discuss "written description" per se in regards to the disclosure of a prior art reference. However, the previous office action did in fact discuss the fact that the Boursnell patent does provide adequate "written description" for the teachings cited by the office according to both section 2121.01 and the newer written description guidelines. It is further noted that neither the MPEP nor the written description guidelines themselves, nor any of the case law previously cited by the applicants suggests that the standard for determining whether the disclosure of a prior art reference meets the level of an anticipatory reference under 35 U.S.C. 102 has been changed from that cited above.

Furthermore, in regards to the previously cited case law concerning "written description", the previous office noted that *Moba B.V. v. Diamond Automation Inc.*, 66 USPQ2d 1429 (Fed. Cir. 2003), which provides extensive commentary on the earlier decisions of the *University of California v. Eli Lilly and Co.* and *Enzo Biochem Inc. v. Gen-Probe Inc.* , concludes that, "Compliance with written description requirement of 35 U.S.C. 112 does not require particular form of disclosure, provided a person of ordinary skill in the art could determine from specification that inventor possessed invention at time of filing" *Moba B.V. v. Diamond Automation Inc.*, page 1430. *Moba B.V. v. Diamond Automation Inc.* further cites *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) for stating, " The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly

allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'". see *Moba B.V. v. Diamond Automation Inc.*, page 1439. Nowhere in any of the cited cases is there the statement that an anticipatory reference must physically make the disclosed invention.

The applicant's grounds of stating that Boursnell lacks written description appears to be that Boursnell, in applicant's opinion, Boursnell does not disclose HSV vectors that contain 2 genes, and further that while Boursnell in column 7-8 does disclose combinations of cytokines and accessory molecules, no specific working examples are provided. These are basically the same arguments addressed in the previous office action. In response, it is first noted that none of applicant's claims are limited to a single HSV amplicon which encodes a gene for an immunostimulatory molecule and a therapeutic gene. Independent Claim 1 for example recites using "one or more species of herpes simplex virus amplicon containing the gene for an immunostimulatory protein and at least one additional therapeutic gene". Thus, the gene for the immunostimulatory protein and the therapeutic gene could be in the same amplicon or in separate amplicons. Independent claim 23 is drawn to a plurality of HSV amplicon species where one species contains the gene for the immunostimulatory protein and a second species contains the therapeutic gene. Boursnell et al. provides substantial direction for making mixtures of recombinant HSV amplicons and packaged HSV vectors which encode an immunomodulatory and/or therapeutic gene (Boursnell et al., column 14, lines 17-41, columns 16-23, Figures 1-6, and column 39-40). It is further noted that the claims in the Boursnell Patent in fact recite methods for using these recombinant HSV vectors to transduce cells (Boursnell et al., columns 39-40, claims 1-16). The Boursnell et al. specification further

specifically teaches transducing tumor cells, including malignant cells of the blood, leukemia cells, and neuroblastoma cells (Boursnell et al., column 6). Further, in claim 11 of the patent, Boursnell teaches HSV encoding a cytokine, an co-stimulatory molecule, or a chemo-attractant. Claim 12 gives GM-CSF, IL-2, IL-12, CD40L, B7.1, and lymphotactin as specific embodiments of the immunomodulatory protein. Please note that under 35 U.S.C. 282, an issued U.S. Patent enjoys the presumption of validity. Case law further states, " Every patent is presumed valid .... The presumption of validity includes a presumption that the patent complies with 112" *National Recovery Technologies Inc. V. Magnetic Separation Systems Inc.*, 49 USPQ 1675 (Fed. Cir. 1999). **Thus, as a matter of law, the Boursnell patent provides written description and enablement for HSV vectors comprising nucleotide sequences encoding immunostimulatory proteins such as cytokines, co-stimulatory molecules, and chemo-attractants, and more specifically IL-2, IL-12, GM-CSF and B7-1.**

Boursnell et al. further teaches that the HSV vectors may encode more than one gene, preferably one or more cytokines, or combinations of cytokines and costimulatory molecules (Boursnell et al., columns 7-8, and column 14, lines 54-60). In particular, please see column 14, lines 54-60, which clearly states that genes for cytokines, immunostimulators, lymphotactin, etc., "can be included in the vectors as single genes or multiple genes, or multiple copies or one or more genes". Column 7 lists examples of useful immunomodulatory protein including Il-2, Il-12, B7-1, RANTES and ICAM-1. Boursnell et al. also teaches that it was well within the skill of the ordinary artisan at the time of filing to make recombinant vectors, including herpes vectors, that encode more than one immunomodulatory gene, such as an antigen and a cytokine (Boursnell et al., columns 2-3, bridging paragraph). From the

detailed description in the Boursnell specification for making a recombinant HSV vector and from the clear indication by Boursnell that methods of making multiply recombinant herpes vectors were known in the art, the Boursnell et al. patent enables the disclosed mixtures of HSV amplicons and the use of those HSV amplicons and vectors to transduce tumor cells. Further, since Boursnell et al. provides sufficient written description for HSV vectors encoding an immunomodulatory molecule as evidenced by the claims in the Boursnell patent, and provided a clear description for making HSV vectors which encode one or more than one immunomodulatory molecule, Boursnell demonstrates possession of the invention as claimed in the instant application.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER